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ZISKA, S EXAMINER

[illegible]1842
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ART UNIT	PAPER NUMBER
1804	8

DATE MAILED: 05/05/93

This [illegible]
COMMISSIONER

☒ This application has been examined ☒ Responsive to communication filed on 1/22/93 ☐ This action is made final.

A shortened statutory period for response to this action is set to expire three (3) month(s), or zero (0) days from the date of this letter. Failure to respond within the period for response will cause the application to become abandoned. 35 U.S.C. 133

Part I THE FOLLOWING ATTACHMENT(S) ARE PART OF THIS ACTION:

1. ☒ Notice of References Cited by Examiner, PTO-892.
2. ☒ Notice re Patent Drawing, PTO-948.
3. ☒ Notice of Art Cited by Applicant, PTO-1449.
4. ☐ Notice of Informal Patent Application, Form PTO-152.
5. ☐ Information on How to Effect Drawing Changes, PTO-1474.
6. ☐ _____

Part II SUMMARY OF ACTION

1. ☒ Claims 1-34 are pending in the application.
   Of the above, claims 1-16, 19, 21-34 are withdrawn from consideration.
2. ☐ Claims _____ have been cancelled.
3. ☐ Claims _____ are allowed.
4. ☒ Claims 17, 18, 20 are rejected.
5. ☐ Claims _____ are objected to.
6. ☐ Claims _____ are subject to restriction or election requirement.
7. ☐ This application has been filed with informal drawings under 37 C.F.R. 1.85 which are acceptable for examination purposes.
8. ☐ Formal drawings are required in response to this Office action.
9. ☐ The corrected or substitute drawings have been received on _____. Under 37 C.F.R. 1.84 these drawings are ☐ acceptable. ☐ not acceptable (see explanation or Notice re Patent Drawing, PTO-948).
10. ☐ The proposed additional or substitute sheet(s) of drawings, filed on _____ has (have) been ☐ approved by the examiner. ☐ disapproved by the examiner (see explanation).
11. ☐ The proposed drawing correction, filed on _____, has been ☐ approved. ☐ disapproved (see explanation).
12. ☐ Acknowledgment is made of the claim for priority under U.S.C. 119. The certified copy has ☐ been received ☐ not been received ☐ been filed in parent application, serial no. _____; filed on _____
13. ☐ Since this application appears to be in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.
14. ☐ Other

EXAMINER'S ACTION

PTOL-326 (Rev. 9-89)

This application should be reviewed for errors.

Claims 17, 18 and 20 are examined in this Office Action; claims 1-16,19 and 21-84 have been withdrawn from consideration due to non-election on the basis of a restriction requirement.

Applicant's election without traverse of Group III, Species A (claims 18 and 20), consisting of claims 17, 18 and 20, in Paper No. 4 is acknowledged.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> "The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention."

The specification is objected to under 35 U.S.C. 112, first paragraph, as failing to provide an adequate written description of the invention and failing to adequately teach how to make and/or use the invention, i.e., failing to provide an enabling disclosure. Applicants have disclosed methods of culturing progenitor cells derived from brain and striatal tissue from mice and have failed to disclose methods of culturing progenitor cells derived from other tissues, such as the blood. Applicants have not presented evidence showing that the culture methods used would be applicable to progenitor cells from other tissues, such as hematopoietic stem cells, for example. Thus, the claims must be limited to progenitor cells derived from brain and striata.

Applicants have disclosed culture of cells derived from the mouse and have failed to disclose evidence that cells derived from other species, such as humans, would be culturable using the same methods or that progenitor cells from other species would be induced to differentiate using the same methods. Note that it is well established that different cells from different

species have different growth and/or differentiation requirements and conditions adequate for one cell type from one species may be inadequate for growth and differentiation of a different cell type from a different species. Thus, the claim must be limited to mouse progenitor cells derived from brain and striata.

Regarding the phrase "isolating a cell from a mammal" is not reflective of the steps actually conducted by Applicants since Applicants first cloned out the cells and then examined the effect of EGF on proliferation and differentiation.

Regarding step (b), of claim 17, Applicants exposed the cells to a particular culture medium containing mouse EGF at a particular concentration and the specification is not enabling for merely exposing the cell to a culture medium containing a growth factor. The claim must be limited to the use of mouse EGF, use of EGF at 20 ng/ml and a particular medium since Applicants have failed to present evidence showing that other growth factors at other concentrations in other medium would allow growth and differentiation of the neural progenitor cells.

In addition, it is well established in the art that the substrate on which the cells are grown is important for achieving differentiation and proliferation (Nakafuku et al, FEBS Letters 315(3): 227, 1993, page 228, column 2 and Weiss, PNAS 83: 2240, 1986) and therefore the claims must be limited to the type of culture substrate shown to be effective in culturing the cells.

Regarding claim 17, Applicants have claimed that EGF induced differentiation of progenitor cells and used antibody to detect the differentiated functions. However, the pictures in the figures are so poor that the results do not support Applicant's assertions. Therefore, Applicants should submit pictures in such a form so as to provide evidence supporting their assertions.

Claim 17 is rejected under 35 U.S.C. 112, first paragraph, for the reasons set forth in the objection to the specification.

Claims 17, 18 and 20 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Regarding claim 17, claim 17 claims a method for the in vitro proliferation of progenitor cells yet the final step include methods for inducing the cell to differentiate. It is not apparent how inducing cells to proliferate would also induce cells to differentiate; indeed, it is known in the art that two process are distinct. Therefore, the claim is vague and unclear since the method detailed in the body of the claim does not correlate with the preamble. Claims 18 and 20 are rejected by virtue of dependency.

Claims 18 and 20 are rejected under 35 U.S.C. 112, first paragraph, as the disclosure is enabling only for claims limited cells derived from brain and striatal tissue and for mouse EGF at a concentration of 20 ng/ml. See MPEP 706.03(n) and 706.03(z). Applicants have disclosed use of murine EGF for differentiation and have disclosed the use of mouse brain cells. Applicants have failed to present evidence showing that mouse EGF would have the same effect on neural cells from other organisms or species and it is well known in the art that receptors may exhibit species specificity for the ligand. Further, Applicants have failed to present evidence showing that EGF at other concentrations would be effective in achieving the same results as set forth in the specification. Therefore, the claims must be limited to mouse EGF and 20 ng/ml and cells derived from brain or striatal tissue. With respect to claim 20, the claim must be limited to mouse brain or striatal cells since Applicants have failed to present evidence showing that human brain or striatal cells would respond in the same manner. Note that it is well established that different cells from different species have different growth and/or differentiation requirements and conditions adequate for one cell type from one species may be inadequate for growth and differentiation of a

different cell type from a different species. Thus, the claim must be limited to mouse progenitor cells derived from brain and striata.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> "A person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States."

Claim 17 is rejected under 35 U.S.C. § 102 (a) as being anticipated by Cattaneo et al. Cattaneo discloses proliferation and differentiation of rat-derived neuronal stem cells regulated by nerve growth factor (Title). Cattaneo discloses use of a growth factor, nerve growth factor, in an in vitro culture system and further discloses that neuronal precursor cells proliferate in response to nerve growth factor, but only after they have been exposed to basic fibroblastic growth factor and that upon withdrawal of nerve growth factor, the proliferative cells differentiate into neurons. Thus, the reference anticipates the claims.

Claim 17 is rejected under 35 U.S.C. § 102 (b) as being anticipated by Morrison et al. Morrison discloses that neurons derived from day old rat brains and cultured in vitro in medium containing EGF have enhanced survival and outgrowth and exhibited differentiated characteristics. Note that the cultured brain cell population obtained is presumed to contain progenitor cells since the cells were able to differentiate, lacking evidence to the contrary. Thus, the reference anticipates the claims.

The following is a quotation of 35 U.S.C. 103 which forms the basis for all obviousness rejections set forth in this Office action:

> A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the

subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Subject matter developed by another person, which qualifies as prior art only under subsection (f) and (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103, the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103.

Claims 18 and 20 are rejected under 35 U.S.C. 103 as being unpatentable over Cattaneo et al as applied to claim 17 above, and further in view of Morrison et al. Claim 17 is rejected under under 35 U.S.C. 102(b) for reasons as stated above. Morrison discloses that neurons cultured in vitro in medium containing EGF have enhanced survival and outgrowth and exhibited differentiated characteristics. Note that Morrison is interpreted not have stem cells or progenitor cells in the isolated population and is cited to disclose use of EGF to induce brain cells to differentiate.

It would have been obvious to one of ordinary skill to culture neural progenitor cells in EGF in order to obtain enhanced survival and differentiated characteristics. Further, it would have been obvious to substitute human or mouse cells for the rat cells of Cattaneo once EGF has been shown to be capable of inducing differentiation and prolonging cell

survival in view of the art recognized desire to obtain cultured neurons for further characterization.

Accordingly, the modification of the method of Cattaneo by using EGF to culture to neuronal stem cells as suggested by Morrison in order to achieve a method for the in vitro proliferation of progenitor cells was within the ordinary skill in the art at the time the claimed invention was made. From the teachings of the references, it is apparent that one of ordinary skill would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole is prima facie obvious, as evidenced by the references, especially in the absence of evidence to the contrary.

Claims 17,18 and 20 are rejected under 35 U.S.C. 103 as being unpatentable over Weiss et al taken with Anchan et al (Abstract) or Morrison et al. Weiss discloses culturing striatal neurons derived from mouse for 14 days in vitro. Weiss further discloses that pretreatment of the culture dishes resulted in rapid neuron attachment and neurite proliferation (Abstract). Weiss discloses that the cell differentiated in culture. Weiss differs from the claims in that the reference fails to disclose exposing the cells to a growth factor during the culture period. However, the secondary references, Morrison or Anchan, cure the deficiency. Morrison or Anchan discloses culturing neurons in the presence of EGF and that EGF enhances survival and process outgrowth of primary cultures (Morrison or Anchan) and further that EGF induced differentiation (Morrison).

Regarding claim 20, it would have been obvious to substitute human cells for the mouse cells of Weiss once EGF has been shown to be capable of inducing differentiation and prolonging cell survival in view of the art recognized desire (Weiss, page 2242, column 1, last paragraph) to obtain cultured neurons for study of anatomical, biochemical and physiological processes in nerve cell function.

Accordingly, the modification of the method of Weiss by using EGF to culture to neuronal stem cells as suggested by Morrison or Anchan in order to achieve a method for the in vitro proliferation and differentiation of progenitor cells was within the ordinary skill in the art at the time the claimed invention was made. From the teachings of the references, it is apparent that one of ordinary skill would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole is prima facie obvious, as evidenced by the references, especially in the absence of evidence to the contrary.

No claim is allowed.

Papers related to this application may be submitted to Group 180 by facsimile transmission. Papers should be faxed to Group 180 via the PTO Fax center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center number is (703)308-4227.

An inquiry concerning this communication should be directed to Examiner Suzanne Ziska, Ph.D., at telephone number 703-308-1217.

Suzanne Ziska
primary
SUZANNE E. ZISKA
PATENT EXAMINER
GROUP 1800
5/1/93